REMARKS

Claim Amendments

Claim 1 has been amended to recite that the rotated support has a different rotational position during an attaching or binding step relative to the support in a prior attaching or binding step. Support for the amendment can be found, for example, in Example 1 and Figure 1.

Claims 1, 14 and 15 have been amended to replace the term "known region" with "localized area". Support for the amendment can be found at page 5, lines 3-15.

No new matter has been added.

Rejection of Claims 1-6 and 14 Under 35 U.S.C. § 103(a)

Claims 1-6 and 14 are rejected under 35 U.S.C. § 103(a) as being obvious over Gamble, *et al.* (U.S. Patent No. 5,981,733). The Examiner states that it would have been obvious to vertically position the substrate of Gamble, *et al.* during the attachment step to thereby insure complete coverage of the activated area and to eliminate problematic bubbles.

Applicants respectfully traverse the rejection. Gamble, *et al.* do not teach or otherwise suggest all of the limitations of the claimed method. Furthermore, there are particular advantages to the instant claimed method that are not taught or suggested by Gamble, *et al.*

Gamble, *et al.* disclose an apparatus for the automated synthesis of molecular arrays on a support. The apparatus includes a jetting device, a reaction chamber to dispense reagents used in the synthesis onto the substrate and optionally a wash station. A positioning system is used to move the support among the jetting device, the reaction chamber and the wash station. The positioning system can be capable of rotating the support parallel and/or perpendicular to the surface of the support.

The nucleic acid array preparation method used by Gamble, *et al.* is described at column 12, line 27 through column 13, line 54. This method begins by horizontally positioning the support over the jetting system, which dispenses a reagent that deprotects locations on the support. The support is then rotated, e.g., to a vertical position to the wash station, and any extra deprotecting reagent is removed and the support is dried. Next, the support is moved to the reaction chamber, where a nucleotide is added to the array. These steps are repeated to form an array. Although the support is rotated into a vertical position to contact the reaction chamber, the rotational position of the support is the same during each of the nucleotide addition steps. This is clearly illustrated in Fig. 7 of Gamble, *et al.* Fig. 7 shows that in moving from the jetting device

to the reaction chamber, the support is first rotated from horizontal to a vertical orientation, and then is rotated such that the longer dimension of the support is oriented along the z-axis. ***The support is then returned to the exact same position for each of the nucleotide addition steps, despite the rotation in between nucleotide addition steps.*** Nowhere do Gamble, *et al.* teach or suggest rotating a substrate such that its rotational position (i.e., position measured about an axis perpendicular to the surface of the substrate) is different in one nucleotide attaching step than its rotational position in another nucleotide attaching step.

Thus, the method taught by Gamble, *et al.* does not teach or otherwise suggest all the limitations of the claimed method. The claimed method of preparing a nucleic acid array on a support requires rotating the support between steps in which a nucleotide is attached, such that the rotational position of the support in one nucleotide attaching step is different from the rotational position of the support in a previous nucleotide attaching step. The rotational position is measured relative to the rotational position of the support in a previous nucleotide attaching step; the rotational position of the support during other method steps is not believed to be critical. In contrast, the rotation used in the method of Gamble, *et al.* always returns the support to the *same rotational position* for nucleotide attaching steps (see Figs. 1 and 7 of Gamble, *et al.*). Thus, Gamble, *et al.* specifically lack a teaching or suggestion related to having the support in different rotational positions during nucleotide attaching steps.

The rotation used in the method of Gamble, *et al.* is solely a consequence of the geometry of the apparatus. That is, the support is rotated so that the support can move among locations in the apparatus (see Fig. 1 of Gamble, *et al.*).

In contrast to Gamble, *et al.*, Example 1 in the subject application demonstrates that rotation of the substrate within the vertical plane results in a support where the attached nucleic acid array has decreased intrasupport variability. In other words, the nucleic acid array is more uniform across the support. Gamble, *et al.* provide no teachings related to the uniformity of a nucleic acid array; in particular there is no teaching or suggestion that varying the rotational position of the support among nucleotide attaching steps can decrease the variability of the array. In fact, Gamble, *et al.* did not even recognize the problem of nucleic acid arrays having significant intrasupport variability. Prior to the present discovery, one of ordinary skill in the art would have had no reason to believe that the recited type of rotation of a support would produce a nucleic acid array having superior properties and would have had no motivation to modify the method of Gamble, *et al.* to include such rotation.

Thus, the claimed method would not have been obvious to one of ordinary skill in the art. Gamble, *et al.* provide no teaching or suggestion for one to carry out a nucleic acid array preparation method where the support is rotated into a different rotational position in a subsequent nucleotide attaching step. Moreover, the subject application makes the surprising discovery that when a nucleic acid array is prepared by a method that includes this step, the resulting nucleic acid array has less intrasupport variability. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 7 and 8 Under 35 U.S.C. § 103(a)

Claims 7 and 8 are rejected under 35 U.S.C. § 103(a) as being obvious over Gamble, *et al.* in view of Bass, *et al.* (U.S. Patent No. 6,440,669). The Examiner states that it would have been obvious to apply the square planar silica support of Bass, *et al.* to the method of Gamble, *et al.* based on its well known use as a support for nucleic acid arrays.

As discussed above, Gamble, *et al.* do not disclose rotating the support into a different rotational position in a subsequent nucleotide attaching step. Similarly, Bass, *et al.* do not disclose rotating the support into a different rotational position in a subsequent nucleotide attaching step. Therefore, Bass, *et al.* do not remedy the deficiencies of Gamble, *et al.*, and Claims 7 and 8 are not obvious over Gamble, *et al.* in view of Bass, *et al.* Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 9-13 Under 35 U.S.C. 103(a)

Claims 9-13 are rejected under 35 U.S.C. § 103(a) as being obvious over Gamble, *et al.* in view of Brennan (U.S. Patent No. 5,985,551). The Examiner states that it would have been obvious to apply the high density array teaching of Brennan to the method of Gamble, *et al.* and to form at least 10, 100, 1000, 10,000 or 100,000 different nucleic acids on the surface of the support.

As discussed above, Gamble, *et al.* do not disclose rotating the support into a different rotational position in a subsequent nucleotide attaching step. Similarly, Brennan does not disclose rotating the support into a different rotational position in a subsequent nucleotide attaching step. Thus, Brennan does not remedy the deficiencies of Gamble, *et al.*, and Claims 9-13 are not obvious over Gamble, *et al.* in view of Brennan. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

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Dated: 11-24-03